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Indicator dispersion in the circulation*

James B. Bassingthwaighle, M.D., Ph.D. and
Section of Physiology, Mayo Clinic, Rochester, Minn

Homer R. Warner, M.D., Ph.D.
Department of Biophysics and Bioengineering, University of Utah, Salt Lake City, Utah

Stewart,[28] in 1897, was one of the first to observe that a bolus became increasingly dispersed as it traveled through the vascular system. He noted that, for a bolus of injected saline, the time between first appearance at the femoral artery and maximal concentration was longer when injection was made into the right ventricle than when made into the left ventricle. This is to be expected whether flow is laminar or turbulent.

In general, dispersion in the circulation is due to four distinct types of processes: (1) velocity profile produced by differences in the velocities of particles at different distances from the wall of a vessel; (2) mixing-pool effects, such as occur in eddies or cardiac chambers which exchange a proportion of their volume with the blood flowing through or past them; (3) random movement of particles backward, forward, and across the stream, as in turbulent flow; and (4) differences in lengths of parallel pathways through the capillary networks of an organ or through different regions of the body.

Velocity profile

The simplest example of nonuniformity of velocities of flowing liquids was demonstrated by Poiseuille in 1840. During steady flow of homogeneous fluids through smooth, straight cylindrical tubes, the velocity is greatest at the axis of the tube and decreases parabolically to zero at the wall. However, this “parabolic laminar flow” cannot occur in the circulation[5] because erythrocytes prohibit the existence of very thin laminae, flow is not steady long enough for disturbances to die away, and vessels are tapered and branching. In parabolic flow, the ratio of maximal to average velocity is 2.0; indicator-dilution studies in circulatory models and dogs,[16] in human subjects,[4,6,25] and in catheters filled with blood[7] result in observed ratios of 1.6 to 1.7. Such values indicate that the velocity profile is more blunt than a parabola, which undoubtedly is due partly to the fact that erythrocytes tend to travel in the center of the stream[8,26] and trap plasma between them.

Mixing pools

The concept of a mixing-pool effect, or exponential washout, was introduced by Hamilton and co-workers,[14] who observed that the decay slopes of concentration-time curves recorded after the injection of a slug of dye could be closely described by a single exponential—that is, the downslope formed a straight line when plotted on semilog paper. A perfect mixing chamber is one in which all of its volume is continuously and instantaneously mixed and the proportion of fluid leaving is F/V, the flow divided by the volume, or the time constant is V/F seconds. Logically, Holt[12] has applied this concept to the washout of indicator injected into a ventricle;

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thus, when the cardiac output is known, the end-diastolic and end-systolic volumes of the ventricle can be calculated. The ratio of stroke volume to end-diastolic volume is less when determined by this method than when estimated by angiocardiography, and, therefore, the completeness of the mixing has been questioned. Application of mixing-pool washout models to the central circulation[17,20,23] is an exercise in curve-fitting—matching a sum of exponentials to recorded dye-dilution curves. Volumes calculated from V/F ("slope volumes," for example) have no apparent physiologic definition.[11,18]

Random movement of particles

After a single injection at an upstream site, a concentration-time curve recorded from the circulation is remarkably like a Gaussian distribution curve skewed to the right, until recirculated indicator mixes with that passing by the sampling point for the first time. Random (Gaussian) dispersion of indicator occurs at the extremes of flow rates. Dispersion by diffusion in fluids flowing very slowly in capillary tubes is Gaussian[10,29] and results in less spread of the bolus than is found with parabolic flow alone. Random dispersion was also observed in highly turbulent flow in oil pipe lines[13] and in water in smooth or rough pipes.[30] The great longitudinal dispersion associated with parabolic flow is due to relatively low velocities in the laminae near the wall of the tube. With very slow flow there is time for indicator to diffuse toward more central, faster flowing laminae. In the violence of turbulent flow the disparity between mean axial velocity and mean velocity near the wall is lessened. Taylor[30] and Hull and Kent[13] found that the dispersion in a straight tube of uniform diameter (as measured by standard deviation of the concentration-time curve, or spread between any pair of chosen concentration levels on the curve) was in proportion to the square root of the distance traveled.

Arriving at the same conclusion completely independently by primarily theoretical reasoning, Sheppard[27] proposed the use of the random walk equation as a mathematical model for dye-dilution curves. The random walk equation is certainly an esthetically pleasing model for circulatory dispersion: it describes the concentration-time curve obtained at a sampling point when a bolus, randomly dispersed with respect to distance, passes by. The model describes dispersion within columns of glass beads but does not describe dye curves from the circulation very closely unless the time origin and rate of spreading are changed to make the curve more skewed. The skewness of recorded dye curves may be explained by either the existence of lower velocities near the wall or by eddy formations acting as mixing pools.

The lagged normal density curve, a model which combines random dispersion with exponential washout, has recently been extensively investigated by Bassingthwaighte, Warner and Wood.[2] The equation has been shown to closely approximate arterial dye curves whether the injection was made into a vena cava or into the aorta, and whether cardiac output or peripheral arterial flow was high or low.[1,3]

Dispersion may be characterized numerically by calculating the variance (the second moment) of the dye curves or the breadth between chosen points on the curve. The data of Korner[15] and of Bassingthwaighte[1] indicate that the standard deviations (the square root of the variance) or the breadths (from appearance time to mean transit time) of dye curves obtained over a wide range of flow rates were linearly related to mean transit time from injection site to sampling site. This indicates that flow has little or no influence on the rate of longitudinal or spatial dispersion. In normal men, dispersion was greatest within the heart and lungs, less in the aorta, and least in the peripheral arterial segment between the femoral and dorsalis pedis arteries.[1] Edwards and Korner[9] noted that, in dogs, dispersion was less in the inferior vena cava than in the thoracic circulation.

Recorded dye curves are the result of dispersion by at least three mechanisms: (1) dispersion produced by the force of injection and by the duration of injection; (2) circulatory dispersion;

and (3) dispersion by the sampling system. If the injection of dye is made somewhere upstream, and dye curves are recorded from two sites simultaneously by means of identical sampling systems with identical sampling flow rates, then one can compute the "transfer function" between the two sampling sites. The transfer function is a description of the dispersion and delay occurring in that segment and is completely independent of dispersion at the site of injection and by the sampling system. The lagged normal density curve serves well as the transfer function for the segment of the arterial system between the femoral and dorsalis pedis arteries of normal men, and the dispersion of the transfer function was, as for the recorded curves, linearly proportional to the mean transit time between the sampling sites, indicating the lack of influence of flow rate (over an eightfold range above normal flows) on the rate of spatial dispersion.[1,3]

Dispersion due to differences in path length

The greater dispersion in the thoracic circulation than in the systemic arterial system[1] is due in part to differences in the lengths of, and the velocities in, different pathways through the capillary bed of the lungs, and in part to the mixing-pool effect of the cardiac chambers. Parrish and co-workers[24] recorded dye curves from the pulmonary arteries and pulmonary veins of dogs and computed the transfer functions between these sites. In general, the transfer functions appeared to be random distributions with some skewing to the right—they were very similar to lagged normal density curves. The latter model has been found to be suitable for describing transfer functions through the lungs, heart, and kidney.[22]

Dispersion is much less through a compact organ than it is over the great differences in path lengths between various organs and, in particular, in the limbs. Moreover, the limbs not only have the longest paths but may also have the slowest velocities: for example, in skin exposed to a cool environment. Nicholes and co-workers[22] have suggested a model for the whole circulation, describing it by transfer functions for specific organs or groups of organs in series and in parallel. Although the details are far from complete, primarily because of the difficulty in distinguishing indicator arriving for the first time through slow paths from that recirculating through faster routes, they have been able to use it to show that exercise increases the proportion of the cardiac output flowing through paths with short transit times.[21] Such analyses also provide a method for determining the flows through these pathways. Flow through specific organs may be estimated if the traversal times of indicator passing through the organ to the central venous circulation can be distinguished from traversal times through other organs.[22]

General comment

The fact that the rate of spatial dispersion in arteries in the legs is unaffected by flow rate[1] strongly suggests that there was no change in flow characteristics in these arteries even when a sixfold to eightfold change in flow rate occurred. Since flow was almost certainly turbulent at the highest flow rates, it is very likely that it also was turbulent at normal flow rates. It must be emphasized that, even in turbulence, the longitudinal velocity is not constant at all points in a cross section, but velocities at the wall may be slower than central velocities; nor is lateral mixing necessarily complete across the cross section (it usually is not). Thus, the existence of stream lines can be expected in arteries in spite of turbulence, and the observation of streaming in the aorta[19] in no way justifies an assumption that the flow is laminar. By definition, in laminar flow the stream lines are infinitely thin. Streaming in highly turbulent flow is very common—for example, the waters of two confluent rivers may remain distinguishable for miles, in spite of Reynolds' numbers of several hundred thousand and obvious localized turbulence.

In spite of the general belief that more dispersion should be produced by turbulence than by laminar flow, mathematical theory and actual observation show that the truth is just the opposite. The presence of turbulence tends to maintain the bolus of indicator in a more intact form, for there is less thickness of slow or stationary fluid at the wall. If this were not so, or if parabolic laminar flow were present, it would almost certainly be impossible to measure either cardiac output or mean circulation times by indicator-dilution techniques in the circulation, for the tails of the curves would be so prolonged that it would be impossible to separate the recirculating indicator from that passing for the first time. By similar reasoning, it is highly unlikely that parabolic laminar flow exists even in the venous system to any great extent, although streaming is much more likely to occur in veins than in arteries.

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